Topic A6: Health and Indoor air epidemiology

INDOOR DAMPNESS AND MOLD AS INDICATORS OF RESPIRATORY HEALTH RISKS, PART 2: A BRIEF UPDATE ON THE EPIDEMIOLOGIC EVIDENCE

Mark J. MENDELL[1, 2,*]

[1]Indoor Air Section, California Department of Public Health, Richmond, CA, US
[2]Indoor Environments Group, Lawrence Berkeley National Laboratory, Berkeley, CA, US

[*]*Corresponding email: mark.mendell@cdph.ca.gov*

Keywords: Dampness, Mold, Fungi, Asthma, Respiratory health

SUMMARY

Evident dampness or mold is consistently associated with increases in multiple respiratory and allergic effects, yet measured microbiologic agents still have limited suggestive associations. Thus, while prevention and remediation of indoor dampness and mold are likely to reduce health risks, current evidence does not support measuring specific indoor microbiologic factors to guide health-protective actions. It is important to identify which specific or aggregate indoor microbial exposures have adverse human health effects, and which have protective effects. Recent findings using molecular methods of microbial identification demonstrate the promise of these methods for developing health-relevant measurements of indoor microbiologic exposures. Meanwhile, quantification of conditions now assessed only subjectively, such as surface moisture or mold odor, may facilitate the prevention of dampness-related health effects.

INTRODUCTION

A prior comprehensive review of the epidemiologic literature on dampness, mold, and health (Mendell et al., 2011) found consistent associations between evident, subjectively assessed indoor dampness or mold and respiratory or allergic health effects. Causal links remained unclear because objectively measured microbiologic organisms, components, or products (all here called “agents”) showed little consistent relationship with health outcomes. This paper (1) examines the previously reviewed findings for evidence that participant bias occurring in studies of weaker design had strong influence on the previous conclusions, because a recent paper (Larsson et al., 2011) has suggested that such bias in most reported studies may have erroneously created apparent associations, and (2) provides a brief update on recent findings since the previous review (Mendell et al., 2011).

METHODS

The 2011 review evaluated the published epidemiologic evidence for causation or association between *qualitative/subjective* assessments of dampness or mold and specific health outcomes. The review separately considered evidence for associations between specific *quantitative* measurements of microbiologic agents and specific health outcomes.

In the current analysis, findings on subjectively assessed dampness or mold were compared across different study designs (in order of decreasing study strength: intervention, prospective, retrospective/case-control, and cross-sectional) as a rough assessment of the potential contribution of study biases to the conclusions of the review. Cross-sectional studies are the most susceptible to various study biases; retrospective studies (including retrospective cross-sectional) are only slightly less susceptible. Prospective and especially intervention studies are the least susceptible to various study biases, and are less likely to use participant assessments of disease and exposure status, a type of data that may contribute bias to many cross-sectional studies of dampness or mold and health (Larsson et al., 2011).

Also, a literature search in PubMed identified articles in the peer-reviewed literature on indoor dampness or mold and health published after those covered in the prior review, and these were examined for findings that would change the prior conclusions.

RESULTS AND DISCUSSION

In the prior review, findings from epidemiologic studies showed evident indoor dampness or mold (e.g., mold odor or visible dampness, water damage, or mold) to be associated consistently with multiple adverse outcomes: increased asthma (both development and exacerbation), respiratory infections, bronchitis, allergic rhinitis, eczema, and various upper and lower respiratory tract symptoms. Studies showed effects in both allergic and non-allergic individuals, and suggested both allergic and non-allergic (presumably pro-inflammatory) mechanisms. Only sparse, suggestive evidence of association with any specific health outcome was available for a few specific, quantified microbiologic agents and these associations, such as for endotoxin and beta-1-D-glucans, were, in part, equivocal.

Table 1 summarizes, by specific study design across the multiple health outcomes studied, the proportions of epidemiologic findings included in the review by Mendell et al. (2011) that showed any increased risk. The 10 health outcomes studied included asthma development, asthma exacerbation, dyspnea, wheeze, bronchitis, cough, respiratory infections (including otitis media), eczema, allergic rhinitis, and upper respiratory tract symptoms (including allergic rhinitis). While the proportion showing associations was slightly smaller for retrospective and prospective studies relative to cross-sectional, these proportions are still very high. The proportion for intervention studies exceeded that for cross-sectional studies. Thus the data do not suggest that bias, whether biased reporting by study subjects or other biases, had a substantial influence on the overall consistent pattern of associations between dampness or mold and multiple health outcomes. (Additional details provided in Appendix Table A1.) Conducting more detailed analyses comparing findings based on occupant- vs. researcher-based health and environmental assessments would answer this question more definitively.

More recently published research generally supports the conclusions of the 2011 review. Some findings suggest potentially promising new directions for research to identify: dampness-related agents causing disease, more successful exposure assessment strategies, and human subgroups with increased susceptibility to dampness-related agents:

- Of the qualitative assessments of dampness or mold studied, mold odor was most strongly correlated with new asthma (Quansah et al., 2012) and rhinitis (Jaakkola et al., 2013).
- Measured wall moisture, in two studies, had dose-related relationships with asthma exacerbation, with ORs up to 7.0 (Williamson et al., 1997; Venn et al., 2003), but this promising approach has not been further pursued (Mendell et al., 2014).

Table 1. Summary of epidemiologic findings on qualitative assessments of dampness or mold, and 10 health outcomes, categorized by study design, from Mendell et al. (2011), Table 1.

Health outcome category	Total number of studies	Odds Ratios (OR) Range	Number of estimates showing any increased risk with D/M [a, b]	Number of total estimates	Proportion of total estimates showing any increased risk with D/M[a, b]
Intervention total	6	---[c]	36	38	95%
Prospective total	36	0.4-7.6	88	105	84%
Retrospective total	17	0.6-4.9	50	60	83%
Cross-sectional total	211	0.3-9.4	570	628	91%

[a] qualitatively assessed dampness or mold

[b] proportion of findings with ORs, risk ratios (RRs), or incidence rate ratios (IRRs) >1.0 (or, for removal of dampness/mold, <1.0), or other types of regression coefficients greater/less than 0 or 1 as appropriate

[c] reported coefficients from linear regression models, not ORs from logistic egression

- Early and diverse microbial exposures, as from farm animals (von Mutius and Vercelli, 2010) or bacteria or fungi in homes (Ege et al., 2011; Dannemiller et al., 2013), seem to protect against the development of allergies or asthma, based on studies using molecular identification assays. The role of specific microorganisms in this process is still unclear.
- Chitin, in all fungal cells, has inflammatory effects in the lung (Van Dyken et al., 2011), and genetic deficiencies in a human enzyme (chitinase) that degrades chitin substantially increase risk of severe asthmatic effects in mold-exposed individuals (Wu et al., 2010).
- Concentrations of several specific fungi, and combined indices of fungi, assessed by quantitative polymerase chain reaction in home dust at child age 12 months, strongly predicted increased risk of asthma development by age 7 years (Reponen et al., 2012).
- Airborne culturable *Penicillium* species have been associated with asthma morbidity in specifically sensitized children, and also in unselected, possibly non-sensitized children (Turyk et al., 2006; Bundy et al., 2009; Pongracic et al.).

CONCLUSIONS

Per available findings, evident dampness or mold is consistently associated with increases in multiple respiratory and allergic effects, yet measured microbiologic agents still have limited suggestive associations, both positive and negative. Thus, while prevention and remediation of indoor dampness and dampness-related microbial agents are likely to reduce health risks, current evidence does not support measuring specific indoor microbiologic factors to guide health-protective actions. It is important to identify which specific or aggregate indoor microbial exposures have adverse human health effects, and which have protective effects. Recent findings using molecular methods of microbial identification demonstrate the promise of these methods for developing health-relevant measurements of indoor microbiologic exposures. Meanwhile, improved quantification of microbial assessments such as measured moisture or qualitative factors such as mold odor may improve prevention of adverse dampness-related health effects.

REFERENCES

Bundy, KW, Gent, JF, Beckett, W, et al. (2009). "Household airborne Penicillium associated with peak expiratory flow variability in asthmatic children." *Ann Allergy Asthma Immunol* **103**(1): 26-30.

Dannemiller, KC, Mendell, MJ, Macher, JM, et al. (2013). "Next-generation DNA sequencing reveals that low fungal diversity in house dust is associated with childhood asthma development." *Indoor air*.

Ege, MJ, Mayer, M, Normand, A-Cc, et al. (2011). "Exposure to Environmental Microorganisms and Childhood Asthma." *New England Journal of Medicine* **364**(8): 701-709.

Jaakkola, MS, Quansah, R, Hugg, TT, et al. (2013). "Association of indoor dampness and molds with rhinitis risk: a systematic review and meta-analysis." *J Allergy Clin Immunol* **132**(5): 1099-1110 e1018.

Larsson, M, Hagerhed-Engman, L, Moniruzzaman, S, et al. (2011). "Can we trust cross-sectional studies when studying the risk of moisture-related problems indoor for asthma in children?" *International Journal of Environmental Health Research* **21**(4): 237-247.

Mendell, MJ, Macher, JM and Kumagai, K (2014). Indoor Dampness and Mold as Indicators of Respiratory Health Risks, Part 3: A Synthesis of Published Data on Indoor Measured Moisture and Respiratory Health. In: Proceedings of Indoor Air 2014, Hong Kong.

Mendell, MJ, Mirer, AG, Cheung, K, et al. (2011). "Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence." *Environ Health Perspect* **119**(6): 748-756.

Pongracic, JA, O'Connor, GT, Muilenberg, ML, et al. (2010). "Differential effects of outdoor versus indoor fungal spores on asthma morbidity in inner-city children." *Journal of Allergy and Clinical Immunology* **125**(3): 593-599.

Quansah, R, Jaakkola, MS, Hugg, TT, et al. (2012). "Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis." *PloS one* **7**(11): e47526.

Reponen, T, Lockey, J, Bernstein, DI, et al. (2012). "Infant origins of childhood asthma associated with specific molds." *J Allergy Clin Immunol* **130**(3): 639-644 e635.

Turyk, M, Curtis, L, Scheff, P, et al. (2006). "Environmental allergens and asthma morbidity in low-income children." *J Asthma* **43**(6): 453-457.

Van Dyken, SJ, Garcia, D, Porter, P, et al. (2011). "Fungal chitin from asthma-associated home environments induces eosinophilic lung infiltration." *The Journal of Immunology* **187**(5): 2261-2267.

Venn, AJ, Cooper, M, Antoniak, M, et al. (2003). "Effects of volatile organic compounds, damp, and other environmental exposures in the home on wheezing illness in children." *Thorax* **58**(11): 955-960.

von Mutius, E and Vercelli, D (2010). "Farm living: effects on childhood asthma and allergy." *Nat Rev Immunol* **10**(12): 861-868.

Williamson, IJ, Martin, CJ, McGill, G, et al. (1997). "Damp housing and asthma: a case-control study." *Thorax* **52**(3): 229-234.

Wu, AC, Lasky-Su, J, Rogers, CA, et al. (2010). "Fungal exposure modulates the effect of polymorphisms of chitinases on emergency department visits and hospitalizations." *American journal of respiratory and critical care medicine* **182**(7): 884.

Appendix Table A1. Summary of epidemiologic findings on qualitative assessments of dampness or mold, and 10 health outcomes, categorized by study design, adapted from Mendell et al. (2011).

Health outcomes with sufficient evidence of association with qualitatively assessed dampness or mold	Total number of studies	OR range	Number of estimates showing any increased risk with D/M [a, b]	Total estimates	Proportion of total estimates showing any increased risk with D/M[a, b]
Intervention Studies					
Asthma exacerbation	3	---[c]	22	22	100%
Dyspnea	1	---[c]	2	2	100%
Wheeze	1	---[c]	7	8	88%
Upper respiratory tract symptoms[d]	1	---[c]	5	6	83%
Prospective Studies					
Asthma development	6	0.6 – 7.1	7	9	78%
Asthma exacerbation	1	3.8 – 7.6	2	2	100%
Wheeze	12	0.7 – 6.2	35	37	95%
Bronchitis	1	0.7 – 3.8	4	5	80%
Cough	2	0.5 – 2.1	7	9	78%
Respiratory infections[e]	5	0.4 – 5.1	14	24	58%
Eczema	2	1.2 – 2.9	3	3	100%
Allergic rhinitis	2	1.2 – 3.2	5	5	100%
Upper respiratory tract symptoms[d]	5	1.0 –3.2	11	11	100%
Retrospective Studies					
Asthma development	8	0.6 – 4.1	29	38	76%
Asthma exacerbation	5	1.5 – 4.9	7	7	100%
Wheeze	2	1.5 – 2.8	9	9	100%
Cough	1	1.2 – 1.9	4	4	100%
Upper respiratory tract symptoms[d]	1	1.0 – 1.3	1	2	50%
Cross-Sectional Studies					
Asthma development	3	1.6-2.2	2	2	100%
Asthma exacerbation	22	1.0 – 7.6	45	47	96%
Dyspnea	15	0.4 – 9.4	56	67	84%
Wheeze	60	0.4 – 8.7	151	164	92%
Bronchitis	11	1.2 – 2.4	19	19	100%
Cough	46	0.2 – 5.7	140	147	95%
Respiratory infections[e]	13	0.5 – 3.1	30	37	81%
Eczema	4	0.3 – 1.9	13	15	87%
Allergic rhinitis	3	0.7 – 3.5	7	8	88%
Upper respiratory tract symptoms[d]	34	0.4 – 5.9	107	122	88%

[a] qualitatively assessed dampness or mold

[b] proportion of findings with ORs, RRs, or IRRS >1.0 (or, for removal of D/M, <1.0), or other coefficients greater/less than 0 or 1 as appropriate

[c] reported coefficients from linear regression models, not ORs from logistic regression

[d] "Upper respiratory tract symptoms" includes findings on allergic rhinitis

[e] "Respiratory infections" includes findings on otitis media